

**Please substitute the following CLAIM set for the pending claim set.**

1. (Currently amended) A method of karyotyping a genome of a test eukaryotic cell,  
comprising:  
  
generating a population of sequence tags from defined portions of the genome of the test  
eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;  
  
enumerating said sequence tags in the population to determine numbers of individual  
sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to  
be present in the genome of the eukaryotic cell are enumerated;  
  
comparing a first number of copies of a plurality of sequence tags enumerated to a second  
number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic  
cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a  
window of sequence tags which are calculated to be contiguous in the genome of the reference  
eukaryotic cell, wherein the window spans about 40 kb, wherein a difference between the first  
number and the second number indicates a karyotypic difference between the test eukaryotic cell and  
the reference eukaryotic cell.
2. (Canceled)
3. (Original) The method of claim 1 wherein the plurality of sequence tags comprises 10 to 500  
contiguous sequence tags.
4. (Original) The method of claim 1 wherein the plurality of sequence tags comprises 50 to  
1000 contiguous sequence tags.
5. (Original) The method of claim 1 wherein the test eukaryotic cell is a human cell.
6. (Canceled)
7. (Previously presented) The method of claim 1 wherein the window spans about 200 kb.

8. (Previously presented) The method of claim 1 wherein the window spans about 600 kb.
9. (Previously presented) The method of claim 1 wherein the window spans about 4 Mb.
10. (Original) The method of claim 1 wherein less than 50 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
11. (Original) The method of claim 1 wherein less than 33 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
12. (Original) The method of claim 1 wherein less than 25 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
13. (Original) The method of claim 1 wherein less than 20 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
14. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated ~~in the step of enumerating;~~

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

15. (Currently amended) The method of claim 1 or 14 wherein the test eukaryotic cell is a cancer cell.

16. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with a hereditary disorder, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

17. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with an infectious disease, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

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enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

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comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

18. (Currently amended) The method of claim 1, 14, 16, or 17 wherein said portions are defined by a first restriction endonuclease cleavage site at a first end of each portion and a second restriction endonuclease cleavage site at a second end of each portion.

19. (Original) The method of claim 18 wherein the first restriction endonuclease cleavage site is a SacI cleavage site.

20. (Currently amended) The method of claim ~~18~~ 19 wherein the second restriction endonuclease cleavage site is a NlaIII cleavage site.

21. (Currently amended) The method of claim 18 wherein recognition or cleavage by the first restriction endonuclease which cleaves at the first cleavage site is sensitive to DNA methylation.

22. (Currently amended) The method of claim 1, 14, 16, or 17 wherein said portions are defined by presence of a BcgI restriction endonuclease recognition site which is flanked by 12 nucleotides on either end.

23. (Currently amended) The method of claim 1, 14, 16, or 17 further comprising:

identifying aneuploidy if (a) sequence tags of one or more autosomes are determined to be present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (b) sequence tags of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (c) sequence tags of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.

24. (Currently amended) The method of claim 1, 14, 16, or 17 wherein the step of enumerating is performed by determining the nucleotide sequence of said sequence tags and recording the number of occurrences of individual sequence tags.

25. (Cancelled)

26. (Cancelled)

27. (Cancelled)

28. (Cancelled)

29. (Cancelled)

30. (Cancelled)

31. (Cancelled)

32. (Cancelled)

33. (Cancelled)

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Canceled)

38. (Currently amended) The method of claim ~~37~~ 51 wherein said portions are defined by a first restriction endonuclease site at a first end of each portion and a second restriction endonuclease site at a second end of each portion.

39. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, wherein said portions are defined by presence of a BcgI restriction endonuclease recognition site which is flanked by 12 nucleotides on either end;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

40. (Currently amended) The method of claim ~~37~~ 39 wherein the window comprises 10 to 500 contiguous tags.

41. (Currently amended) The method of claim ~~37~~ 39 wherein the window comprises 50 to 1000 contiguous tags.

42. (Currently amended) The method of claim ~~37~~ 39 wherein the test eukaryotic cell is a human cell.

43. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 40 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

44. (Currently amended) The method of claim ~~37~~ 43 wherein the window spans about 200 kb.

45. (Currently amended) The method of claim ~~37~~ 43 wherein the window spans about 600 kb.

46. (Currently amended) The method of claim ~~37~~ 43 wherein the window spans about 4 Mb.

47. (Currently amended) The method of claim ~~37~~ 43 wherein less than 50 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

48. (Currently amended) The method of claim ~~37~~ 43 wherein less than 33 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

49. (Currently amended) The method of claim ~~37~~ 43 wherein less than 25 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

50. (Currently amended) The method of claim ~~37~~ 43 wherein less than 20 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

51. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

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generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

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enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated ~~in the step of~~ enumerating;

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comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of



sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

52. (Currently amended) The method of claim ~~37~~ 51 wherein the test eukaryotic cell is a cancer cell.

53. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with a hereditary disorder comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

54. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the cell is a cell of a person with an infectious disease, comprising:

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generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

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enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

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comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality

55. (Currently amended) The method of claim ~~37~~ 38 wherein the first restriction endonuclease recognition site is a *SacI* recognition site.

56. (Currently amended) The method of claim ~~38~~ 55 wherein the second restriction endonuclease recognition site is a *NlaIII* recognition site.

57. (Currently amended) The method of claim ~~38~~ 51 wherein recognition or cleavage by ~~the~~ a first restriction endonuclease is sensitive to DNA methylation, wherein said first restriction endonuclease cleaves at said one or two restriction endonuclease recognition sites.

58. (Currently amended) The method of claim ~~37~~ 51 wherein the step of enumerating is performed by determining the nucleotide sequence of said sequence tags and recording the number of occurrences of individual sequence tags.

59. (Canceled)

- 60. (Canceled)
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85. (Canceled)

86. (Canceled)

87. (Previously Presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating copies of said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

88. (Canceled)

89. (Previously Presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population;

comparing the first number of the plurality of copies of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

90. (Previously presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome, wherein the window spans about 200 kb;

comparing a first number of pieces enumerated within a plurality of windows for the test eukaryotic cell to a second number of pieces enumerated within the plurality of windows for a reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

91. (Canceled)